TITLE 22. EXAMINING BOARDS
Part 15. Texas State Board of Pharmacy
Chapter 291. Pharmacies
Subchapter A. All Classes of Pharmacy

22 TAC §291.26

The Texas State Board of Pharmacy proposes new §291.26 concerning Pharmacies Compounding Sterile Pharmaceuticals. The new section, if adopted, will outline operating standards for pharmacies that compound sterile pharmaceuticals and will implement the recommendations of the Board appointed Task Force on Compounding.

Gay Dodson, R.Ph., Executive Director/Secretary, has determined that, for the first five-year period the rule is in effect, there will be no fiscal implications for state government as a result of enforcing or administering the rule. There are no anticipated fiscal implications for local government.

Ms. Dodson has determined that, for each year of the first five-year period the rule will be in effect, the public benefit anticipated as a result of enforcing the rule will be the establishing of standards for the compounding of sterile pharmaceuticals by pharmacies. There is no fiscal impact anticipated for small or large businesses or to other entities who are required to comply with this section.

A public hearing to receive comments on the proposed new rule will be held at 9:00 a.m. on Tuesday, November 18, 2003, at the Health Professions Council Board Room, 333 Guadalupe Street, Tower II, Room 2-225, Austin, Texas 78701. Persons planning to present comments to the Board are asked to provide a written copy of their comments prior to the hearing or bring 20 copies to the hearing. Written comments on the new rule may be submitted to Allison Benz, R.Ph., M.S., Director of Professional Services, 333 Guadalupe Street, Suite 3-600, Austin, Texas, 78701, FAX: 512/305-8082, E-mail: allison.benz@tsbp.state.tx.us. Comments must be received by 5 p.m., November 12, 2003.

The new rule is proposed under sections 551.002 and 554.051 of the Texas Pharmacy Act (Chapters 551-566 and 568-569, Texas Occupations Code). The Board interprets section 551.002 as authorizing the agency to protect the public through the effective control and regulation of the practice of pharmacy. The Board interprets section 554.051(a) as authorizing the agency to adopt rules for the proper administration and enforcement of the Act. The Board interprets section 554.051(b) as authorizing the agency to make a rule concerning the operation of a licensed pharmacy located in this state applicable to a pharmacy licensed by the board that is located in another state, if the board determines the rule is necessary to protect the health and welfare of the citizens of this state.

The statutes affected by this rule: Chapters 551-566 and 568-569, Texas Occupations Code.

The agency hereby certifies that the proposed new rule has been reviewed by legal counsel and found to be a valid exercise of the agency's authority.

§291.26. Pharmacies Compounding Sterile Pharmaceuticals

(a) Purpose. The purpose of this section is to provide standards for the compounding of sterile pharmaceuticals by all in Class A (Community), Class B (Nuclear), Class C (Institutional) and Class E (Non-resident) pharmacies. Pharmacies compounding sterile pharmaceuticals shall comply with all requirements for their specific license classification and this section.

(b) Definitions. In addition to the definitions for specific license classifications, the following words and terms, when used in this section, shall have the following meanings, unless the context clearly indicates otherwise.

(1) ACPE - The American Council on Pharmaceutical Education.

(2) Airborne particulate cleanliness class - The level of cleanliness specified by the maximum allowable number of particles per cubic foot of air as specified in Federal Standard 209E, et seq. or by the International Organization of Standardization (ISO) Classification. For example:

(A) Class 100 (ISO Class 5) is an atmospheric environment which contains less than 100 particles 0.5 microns in diameter per cubic foot of air;
(B) Class 10,000 (ISO Class 7) is an atmospheric environment which contains less than 10,000 particles 0.5 microns in diameter per cubic foot of air; and
(C) Class 100,000 (ISO Class 8) is an atmospheric environment which contains less than 100,000 particles 0.5 microns in diameter per cubic foot of air.

(3) Ancillary supplies - Supplies necessary for the administration of compounded sterile pharmaceuticals.

(4) Aseptic preparation - The technique involving procedures designed to preclude contamination of drugs, packaging, equipment, or supplies by microorganisms during processing.

(5) Automated compounding or counting device - An automated device that compounds, measures, counts, and or packages a specified quantity of dosage units for a designated drug product.

(6) Batch preparation compounding - Compounding of multiple sterile-product units, in a single discrete process, by the same individual(s), carried out during one limited time period. Batch preparation/compounding does not include the preparation of multiple sterile-product units pursuant to patient specific medication orders.

(7) Beyond-use date - The date after which a compounded preparation should not be used and is determined from the date the preparation was compounded.

(8) Biological Safety Cabinet - Containment unit suitable for the preparation of low to moderate risk agents where there is a need for protection of the product, personnel, and environment, according to National Sanitation Foundation (NSF) Standard 49.

(9) Clean room - A room in which the concentration of airborne particles is controlled and there are one or more clean zones according to Federal Standard 209E, et seq.

(10) Clean zone - A defined space in which the concentration of airborne particles is controlled to meet a specified airborne particulate cleanliness class.

(11) Component - Any ingredient intended for use in the compounding of a drug product, including those that may not appear in such product.

(12) Compounding - The preparation, mixing, assembling, packaging, or labeling of a drug or device:
(A) as the result of a practitioner's prescription drug or medication order or initiative based on the practitioner-patient pharmacist relationship in the course of professional practice;
(B) in anticipation of prescription drug or medication orders based on routine, regularly observed prescribing patterns; or
(C) for the purpose of or as an incident to research, teaching, or chemical analysis and not for sale or dispensing.

(13) Controlled area - A controlled area is the area designated for preparing sterile pharmaceuticals.

(14) Critical site - Any opening providing a direct pathway between a sterile product and the environment or any surface coming in direct contact with the product and the environment.

(15) Cytotoxic - A pharmaceutical that has the capability of killing living cells.

(16) Device - An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component part or accessory, that is required under federal or state law to be ordered or prescribed by a practitioner.

(17) Process validation - Documented evidence providing a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.

(18) SOPs - Standard operating procedures.

(19) Quality assurance - The set of activities used to assure that the process used in the preparation of sterile drug products lead to products that meet predetermined standards of quality.

(20) Quality control - The set of testing activities used to determine that the ingredients, components (e.g., containers), and final sterile pharmaceuticals prepared meet predetermined requirements with respect to identity, purity, non-pyrogenicity, and

sterility.

(21) Sterile pharmaceutical - A dosage form free from living micro-organisms.

(22) USP/NF - the United States Pharmacopeia/National Formulary

(c) Personnel.

(1) Pharmacist-in-charge.

(A) General. The pharmacy shall have a pharmacist-in-charge in compliance with the specific license classification of the pharmacy.

(B) Responsibilities. In addition to the responsibilities for the specific class of pharmacy, the pharmacist-in-charge shall have the responsibility for, at a minimum, the following concerning sterile compounding:

(i) developing a system to assure that all pharmacy personnel responsible for compounding and/or supervising the compounding of sterile pharmaceuticals within the pharmacy receive appropriate education and training and competency evaluation;

(ii) determining that all pharmacists involved in compounding sterile pharmaceuticals obtain continuing education appropriate for the type of compounding done by the pharmacist;

(iii) supervising a system to assure appropriate procurement of drugs and devices and storage of all pharmaceutical materials including pharmaceuticals, components used in the compounding of pharmaceuticals, and drug delivery devices;

(iv) assuring that the equipment used in compounding is properly maintained;

(v) developing a system for the disposal and distribution of drugs from the pharmacy;

(vi) developing a system for bulk compounding or batch preparation of drugs;

(vii) developing a system for the compounding, sterility assurance, quality assurance and quality control of sterile pharmaceuticals; and

(viii) assuring that the pharmacy has a system to dispose of cytotoxic and/or biohazardous waste in a manner so as not to endanger the public health.

(2) Pharmacists. Special requirements for sterile compounding.

(A) All pharmacists engaged in compounding shall:

(i) possess the education, training, and proficiency necessary to properly and safely perform compounding duties undertaken or supervised; and

(ii) obtain continuing education appropriate for the type of compounding done by the pharmacist.

(B) A pharmacist shall inspect and approve all components, drug product containers, closures, labeling, and any other materials involved in the compounding process.

(C) A pharmacist shall review all compounding records for accuracy and conduct in-process and final checks to assure that errors have not occurred in the compounding process.

(D) A pharmacist is responsible for the proper maintenance, cleanliness, and use of all equipment used in the compounding process.

(E) A pharmacist shall be accessible at all times to respond to patients' and other health professionals' questions and needs. Such access may be through a telephone which is answered 24 hours a day.

(3) Pharmacy technicians. Pharmacy technicians may compound sterile pharmaceuticals provided the pharmacy technicians:

(A) are either certified pharmacy technicians or technician trainees;

(B) have completed the education and training specified in paragraph (4) of this subsection; and

(C) are supervised by a pharmacist who has completed the training specified in paragraph (4) of this subsection, conducts in-process and final checks, and affixes his or her initials to the appropriate quality control records.

(4) Special education, training, and evaluation requirements for pharmacy personnel compounding or responsible for the direct supervision of pharmacy personnel compounding sterile pharmaceuticals.

(A) General.

(i) All pharmacy personnel preparing sterile pharmaceuticals shall receive didactic and experiential training and competency evaluation through demonstration, testing (written or practical) as outlined by the pharmacist-in-charge and described in the policy and procedure or training manual. Such training shall include instruction and experience in the following areas:
(I) aseptic technique;
(II) critical area contamination factors;
(III) environmental monitoring;
(IV) facilities;
(V) equipment and supplies;
(VI) sterile pharmaceutical calculations and terminology;
(VII) sterile pharmaceutical compounding documentation;
(VIII) quality assurance procedures;
(IX) aseptic preparation procedures including proper gowning and gloving technique;
(X) handling of cytotoxic and hazardous drugs, if applicable; and
(XI) general conduct in the controlled area.

(ii) The aseptic technique of each person compounding or responsible for the direct supervision of personnel compounding sterile pharmaceuticals shall be observed and evaluated as satisfactory through written or practical tests and process validation and such evaluation documented.

(iii) Although process validation may be incorporated into the experiential portion of a training program, process validation must be conducted at each pharmacy where an individual compounds sterile pharmaceuticals. No product intended for patient use shall be compounded by an individual until the on-site process validation test indicates that the individual can competently perform aseptic procedures, except that a pharmacist may temporarily compound sterile pharmaceuticals and supervise pharmacy technicians compounding sterile pharmaceuticals without process validation provided the pharmacist:
(I) has completed a recognized course in an accredited college of pharmacy or a course sponsored by an American Council on Pharmaceutical Education approved provider which provides 20 hours of instruction and experience in the areas listed in this subparagraph; and
(II) completes the on-site process validation within seven days of commencing work at the pharmacy.

(iv) Process validation procedures for assessing the preparation of specific types of sterile pharmaceuticals shall be representative of all types of manipulations, products, and batch sizes that personnel preparing that type of pharmaceutical are likely to encounter.

(v) The pharmacist-in-charge shall assure continuing competency of pharmacy personnel through in-service education, training, and process validation to supplement initial training. Personnel competency shall be evaluated:
(I) during orientation and training prior to the regular performance of those tasks;
(II) whenever the quality assurance program yields an unacceptable result;
(III) whenever unacceptable techniques are observed; and
(IV) at least on an annual basis.

(B) Pharmacists.
(i) All pharmacists who compound sterile pharmaceuticals or supervise pharmacy technicians compounding sterile pharmaceuticals shall:
(I) initially and every seven years thereafter, complete through a single course, a minimum of 20 hours of instruction and

experience in the areas listed in subparagraph (A) of this paragraph. Such training shall be completed at least every seven years and may be obtained through:

(-a-) completion of a structured on-the-job didactic and experiential training program at this pharmacy which provides 20 hours of instruction and experience in the areas listed in paragraph (1) of this subsection. Such training may not be transferred to another pharmacy unless the pharmacies are under common ownership and control and use a common training program; or

(-b-) completion of a recognized course in an accredited college of pharmacy or a course sponsored by an American Council on Pharmaceutical Education approved provider which provides 20 hours of instruction and experience in the areas listed in subparagraph (A) of this paragraph; and

(II) possess knowledge about:

(-a-) aseptic processing;

(-b-) quality control and quality assurance as related to environmental, component, and end-product testing;

(-c-) chemical, pharmaceutical, and clinical properties of drugs;

(-d-) container, equipment, and closure system selection; and

(-e-) sterilization techniques.

(ii) The required experiential portion of the training programs specified in this subparagraph must be supervised by an individual who has already completed training as specified in subparagraph (B) or (C) of this paragraph.

(C) Pharmacy technicians. In addition to qualifications for specific license classifications all pharmacy technicians who compound sterile pharmaceuticals shall:

(i) have a high school or equivalent education;

(ii) have initial training obtained either through completion of:

(I) a single course, a minimum of 40 hours of instruction and experience in the areas listed in subparagraph (A) of this paragraph. Such training may be obtained through:

(-a-) completion of a structured on-the-job didactic and experiential training program at this pharmacy which provides 40 hours of instruction and experience in the areas listed in subparagraph (A) of this paragraph. Such training may not be transferred to another pharmacy unless the pharmacies are under common ownership and control and use a common training program; or

(-b-) completion of a course sponsored by an ACPE approved provider which provides 40 hours of instruction and experience in the areas listed in subparagraph (A) of this paragraph; or

(II) a training program which is accredited by the American Society of Health-System Pharmacists (formerly the American Society of Hospital Pharmacists). Individuals enrolled in training programs accredited by the American Society of Health-System Pharmacists may compound sterile pharmaceuticals in a licensed pharmacy provided:

(-a-) the compounding occurs only during times the individual is assigned to a pharmacy as a part of the experiential component of the American Society of Health-System Pharmacists training program;

(-b-) the individual is under the direct supervision of and responsible to a pharmacist who has completed training as

specified in subparagraph (B) of this paragraph; and

(-c-) the supervising pharmacist conducts in-process and final checks; and

(iii) repeat the training specified in clause (ii) of this subparagraph at least every seven years.

(iv) acquire the required experiential portion of the training programs specified in this subparagraph under the supervision of an individual who has already completed training as specified in subparagraph (B) or (C) of this paragraph.

(D) Documentation of Training. A written record of initial and in-service training and the results of written or practical testing and process validation of pharmacy personnel shall be maintained and contain the following information:

(i) name of the person receiving the training or completing the testing or process validation;

(ii) date(s) of the training, testing, or process validation;

(iii) general description of the topics covered in the training or testing or of the process validated;

(iv) name of the person supervising the training, testing, or process validation; and

(v) signature (first initial and last name or full signature) of the person receiving the training or completing the testing or process validation and the pharmacist-in-charge or other pharmacist employed by the pharmacy and designated by the pharmacist-in-charge as responsible for training, testing, or process validation of personnel.

(d) Operational Standards.

(1) General Requirements.

(A) Sterile drug products may be compounded in licensed pharmacies:

(i) upon presentation of a practitioner’s prescription drug or medication order, or an initiative based on a valid pharmacist/patient/prescriber relationship; or

(ii) i n anticipation of future prescription drug or medication orders based on routine, regularly observed prescribing patterns.

(B) Sterile compounding in anticipation of future prescription drug or medication orders must be based upon a history of receiving valid prescriptions issued within an established pharmacist/patient/prescriber relationship, provided that in the pharmacist's professional judgment the quantity prepared is stable for the anticipated shelf time.

(i) The pharmacist's professional judgment shall be based on the criteria used to determine a beyond-use date outlined in paragraph (5)(C) of this subsection.

(ii) Documentation of the criteria used to determine the stability for the anticipated shelf time must be maintained with the sterile compounding record.

(iii) Any product compounded in anticipation of future prescription drug or medication orders shall be labeled. Such label shall contain:

(I) name and strength of the compounded medication or list of the active ingredients and strengths;

(II) facility's lot number;

(III) beyond-use date as determined by the pharmacist using appropriate documented criteria as outlined in clause (i) of this subparagraph;

(IV) quantity or amount in the container;

(V) appropriate ancillary instructions, such as storage instructions or cautionary statements, including cytotoxic warning labels where appropriate; and

(VI) device-specific instructions, where appropriate.

(C) Commercially available products may be compounded for dispensing or

administration to individual patients or for distribution to practitioners provided the following conditions are met:

(i) the commercial product is not reasonably available from normal distribution channels in a timely manner to meet patient's needs; and

(ii) the prescribing practitioner has requested that the drug be compounded.

(D) Pharmaceuticals must be compounded for the exclusive use of the pharmacy where the products are compounded except that a pharmacy may enter into an agreement to compound and dispense prescription/medication orders for another pharmacy provided the pharmacy complies with the provisions of §291.37 of this title (relating to Centralized Prescription Dispensing). Compounded pharmaceuticals may not be distributed for resale, including distribution to pharmacies under common ownership or control. This restriction does not apply to distributions of compounded pharmaceuticals to a practitioner under the following conditions.

(i) The practitioner requests the compounded pharmaceutical for administration, but not dispensing, to the practitioner's patients.

(ii) The quantity of all compounded pharmaceuticals distributed to all practitioners during the previous 12 months pursuant to this exception does not exceed 5% of all prescriptions compounded and dispensed during the previous 12 months. For the purpose of this exception, distributions to practitioners shall not be included in the 5% if the pharmacy receives and documents within 30 days of distribution, the name of the patient to whom the compounded pharmaceutical was administered.

(iii) Products compounded for physician administration to patients shall be labeled. Such label shall contain:

(I) the statement: "For Office Use Only";

(II) name and strength of the compounded medication or list of the active ingredients and strengths;

(III) facility's control number;

(IV) beyond-use date as determined by the pharmacist using appropriate documented criteria as outlined in paragraph (5)(C) of this subsection; and

(V) quantity or amount in the container.

(E) Compounding pharmacies/pharmacists may advertise and promote the fact that they provide sterile prescription compounding services, which may include specific drug products.

(2) Risk levels for compounded sterile pharmaceuticals.

(A) Low-risk level compounded sterile pharmaceuticals.

(i) Low-risk level compounded sterile pharmaceuticals are those compounded under all of the following conditions.

(I) Compounding with aseptic manipulations entirely within a Class 100 (ISO Class 5) or better air quality using only sterile ingredients, products, components, and devices.

(II) Compounding involves only transfer, measuring, and mixing manipulations with closed or sealed packaging systems that are performed promptly and attentively.

(III) Manipulations are limited to aseptically opening ampuls, penetrating sterile stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile administration devices and packages of other sterile products.

(ii) Examples of low-risk compounding include the following.

(I) Single transfers of sterile dosage forms from ampuls, bottles, bags, and vials using sterile syringes with sterile needles, other administration devices, and other sterile containers. The contents of ampuls require sterile filtration to remove glass particles.

(II) Manually measuring and mixing no more than three manufactured

products to compound drug admixtures and nutritional solutions.

(B) Medium-risk level compounded sterile pharmaceuticals.

(i) Medium-risk level compounded sterile pharmaceuticals are those compounded aseptically under low-risk conditions and one or more of the of the following conditions exists.

(I) Multiple individual or small doses of sterile products are combined or pooled to prepare a compounded sterile pharmaceutical that will be administered either to multiple patients or to one patient on multiple occasions.

(II) The compounding process includes complex aseptic manipulations other than the single-volume transfer.

(III) The compounding process requires unusually long duration, such as that required to complete the dissolution or homogenous mixing.

(IV) The sterile compounded pharmaceutical's do not contain broad-spectrum bacteriostatic substances, and they are administered over several days.

(ii) Examples of medium-risk compounding include the following.

(I) Compounding of total parenteral nutrition fluids using a manual or automated device during which there are multiple injections, detachments, and attachments of nutrient source products to the device or machine to deliver all nutritional components to a final sterile container.

(II) Filling of reservoirs of injection and infusion devices with multiple sterile drug products, and evacuations of air from those reservoirs before the filled device is dispensed.

(III) Filling of reservoirs of injection and infusion devices with volumes of sterile drug solutions that will be administered over several days at ambient temperatures between 15 and 30 degrees Celsius (59 and 86 degrees Fahrenheit).

(IV) Transfer of volumes from multiple ampuls or vials into a single, final sterile container or product.

(C) High-risk level compounded sterile pharmaceuticals.

(i) High-risk level compounded sterile pharmaceuticals are those compounded under any of the following conditions.

(I) Nonsterile ingredients, including manufactured products are incorporated, or a nonsterile device is employed before terminal sterilization.

(II) Sterile ingredients, components, devices, and mixtures are exposed to air quality inferior to Class 100 (ISO Class 5). This includes storage in environments inferior to Class 100 (ISO Class 5) of opened or partially used packages of manufactured sterile products that lack antimicrobial preservatives.

(III) Nonsterile preparations are exposed no more than 6 hours before being sterilized.

(IV) It is assumed, and not verified by examination of labeling and documentation from suppliers or by direct determination, that the chemical purity and content strength of ingredients meet their original or compendial specifications in unopened or in opened packages of bulk ingredients.

(ii) Examples of high-risk compounding include the following.

(I) Dissolving nonsterile bulk drug and nutrient powders to make solutions, which will be terminally sterilized.

(II) Sterile ingredients, components, devices, and mixtures are exposed to air quality inferior to Class 100 (ISO Class 5). This includes storage in environments inferior to Class 100 (ISO Class

5) of opened or partially used packages of manufactured sterile products that lack antimicrobial preservatives.

(III) Measuring and mixing sterile ingredients in nonsterile devices before sterilization is performed.

(IV) Assuming, without appropriate evidence or direct determination, that packages of bulk ingredients contain at least 95% by weight of their active chemical moiety and have not been contaminated or adulterated between uses.

(3) Environment.

(A) Special requirements for the compounding of sterile pharmaceuticals. When the pharmacy compounds sterile pharmaceuticals, the following is applicable.

(i) Controlled area. The pharmacy shall have a designated controlled area for the compounding of sterile pharmaceuticals that is functionally separate from areas for the preparation of non-sterile pharmaceuticals and is constructed to minimize the opportunities for particulate and microbial contamination. This controlled area for the preparation of sterile pharmaceuticals shall:

(I) have a controlled environment that is aseptic or contains an aseptic environmental control device(s). If the aseptic environmental control device is located within the controlled area, the controlled area must extend a minimum of six feet from the device and clearly marked to identify the separation between the controlled and non-controlled area;

(II) be clean, well lighted, and of sufficient size to support sterile compounding activities;

(III) be used only for the compounding of sterile pharmaceuticals;

(IV) be designed to avoid outside traffic and air flow;

(V) be designed such that hand sanitizing and gowning occurs outside the controlled area but is accessible without use of the hands of the compounding personnel;

(VI) have non-porous and washable floors or floor covering to enable regular disinfection;

(VII) be ventilated in a manner not interfering with aseptic environmental control conditions;

(VIII) have hard cleanable walls and ceilings (acoustical ceiling tiles that are coated with an acrylic paint are acceptable);

(IX) have drugs and supplies stored on shelving areas above the floor to permit adequate floor cleaning; and

(X) contain only the appropriate compounding supplies and not be used for bulk storage for supplies and materials.

(ii) Aseptic environment control device(s). The pharmacy shall prepare sterile pharmaceuticals in an appropriate aseptic environmental control device(s) or area, such as a laminar air flow hood, biological safety cabinet, clean room which is capable of maintaining at least Class 100 (ISO Class 5) conditions during normal activity, or other aseptic environmental control devices that produce Class 100 (ISO Class 5) environmental conditions or better. The aseptic environmental control device(s) shall:

(I) be certified by an independent contractor according to Federal Standard 209E, et seq, for operational efficiency at least every six months or when it is relocated; and

(II) have pre-filters inspected periodically and replaced as needed, in accordance with written policies and procedures, and the inspection and/or replacement date documented.

(iii) Automated compounding or counting device. If automated compounding or counting devices are used, the pharmacy shall have a method to calibrate and verify the accuracy of automated compounding or counting devices used in aseptic processing and document the calibration and

verification on a routine basis.

(iv) Cytotoxic drugs. In addition to the requirements specified in clause (ii) of this subparagraph, if the product is also cytotoxic, the following is applicable.

(I) General.

(-a-) All personnel involved in the compounding of cytotoxic products shall wear appropriate protective apparel, such as masks, gloves, and gowns or coveralls with tight cuffs.

(-b-) Appropriate safety and containment techniques for compounding cytotoxic drugs shall be used in conjunction with aseptic techniques required for preparing sterile pharmaceuticals.

(-c-) Disposal of cytotoxic waste shall comply with all applicable local, state, and federal requirements.

(-d-) Prepared doses of cytotoxic drugs must be dispensed, labeled with proper precautions inside and outside, and distributed in a manner to minimize patient contact with cytotoxic agents.

(II) Aseptic environment control device(s).

(-a-) Cytotoxic drugs must be prepared in a vertical flow biological safety cabinet, or other aseptic environmental control devices that produce Class 100 (ISO Class 5) environmental conditions or better and provide protection from cytotoxic products to personnel.

(-b-) If the aseptic environment control device is also used to prepare non-cytotoxic sterile pharmaceuticals, the device must be thoroughly cleaned prior to its use to prepare non-cytotoxic sterile pharmaceuticals.

(B) Security requirements. The pharmacy may authorize personnel to gain access to that area of the pharmacy containing dispensed sterile pharmaceuticals, in the absence of the pharmacist, for the purpose of retrieving dispensed prescriptions to deliver to patients. If the pharmacy allows such after-hours access, the area containing the dispensed sterile pharmaceuticals shall be an enclosed and lockable area separate from the area containing undispensed prescription drugs. A list of the authorized personnel having such access shall be in the pharmacy's policy and procedure manual.

(4) Equipment and supplies. Pharmacies compounding sterile pharmaceuticals shall have the following equipment and supplies:

(A) a system or device (i.e., thermometer) to monitor the temperature daily to ensure that proper storage requirements are met if sterile pharmaceuticals are stored in the refrigerator;

(B) a Class A prescription balance, or analytical balance and weights. Such balance shall be properly maintained and inspected at least every three years by the Texas State Board of Pharmacy;

(C) have equipment and utensils necessary for the proper compounding of prescription drug or medication orders. Such equipment and utensils used in the compounding process shall be:

(i) of appropriate design, appropriate capacity, and be operated within designed operational limits;

(ii) of suitable composition so that surfaces that contact components, in-process material, or drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond acceptable standards;

(iii) cleaned and sanitized immediately prior to each use; and

(iv) routinely inspected, calibrated (if necessary), or checked to ensure proper performance;

(D) appropriate disposal containers for used needles, syringes, etc., and if

applicable, cytotoxic waste from the preparation of chemotherapeutic agents, and/or biohazardous waste;

(E) temperature controlled delivery containers;

(F) infusion devices, if applicable; and

(G) all necessary supplies, including:

(i) disposable needles, syringes, and other aseptic mixing;

(ii) disinfectant cleaning solutions;

(iii) hand washing agents with bactericidal action;

(iv) disposable, lint free towels or wipes;

(v) appropriate filters and filtration equipment;

(vi) cytotoxic spill kits, if applicable; and

(vii) masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as applicable.

(5) Labeling. In addition to the labeling requirements for the pharmacy's specific license classification, the label dispensed or distributed pursuant to a prescription drug or medication order shall contain the following.

(A) The brand name, official name, or the principle active ingredients of the compounded pharmaceutical.

(B) A statement that the preparation has been compounded by the pharmacy.

(C) A beyond-use date after which the compounded pharmaceutical should not be used. In the absence of stability testing the beyond-use date shall be limited by the risk level of the compounded pharmaceutical and the storage temperature as follows as long as the chemical stability of the drug permits.

(i) Low-risk level compounded sterile pharmaceuticals.

(I) 48 hours if stored at room temperature.

(II) 14 days if stored in cold temperatures (2 - 8 degrees Celsius (36 - 46 degrees Fahrenheit)).

(III) 45 days if stored frozen (minus 20 degrees Celsius (minus 4 degrees Fahrenheit) or colder)

(ii) Medium-risk level compounded sterile pharmaceuticals.

(I) 30 hours if stored at room temperature.

(II) 7 days if stored in cold temperatures (2 - 8 degrees Celsius (36 - 46 degrees Fahrenheit)).

(III) 45 days if stored frozen ((minus 20 degrees Celsius (minus 4 degrees Fahrenheit) or colder)

(iii) High-risk level compounded sterile pharmaceuticals.

(I) 24 hours if stored at room temperature.

(II) 3 days if stored in cold temperatures (2 - 8 degrees Celsius (36 - 46 degrees Fahrenheit)).

(III) 45 days if stored frozen ((minus 20 degrees Celsius (minus 4 degrees Fahrenheit) or colder)

(D) If the sterile pharmaceutical is compounded in a batch, the following should also be included on the label.

(i) unique lot number assigned to the batch;

(ii) quantity;

(iii) appropriate ancillary instructions, such as storage instructions or cautionary statements, including cytotoxic warning labels where appropriate; and

(iv) device-specific instructions, where appropriate.

(6) Written drug information. Written information about the compounded drug or its major active ingredient(s) shall be given to the patient at the time of dispensing. A statement which indicates that the product was compounded by the pharmacy must be included in this written information. If there is no written information available, the patient should be advised in writing that the drug has been compounded and how to contact a pharmacist, and if appropriate the prescriber, concerning the drug.

(7) Pharmaceutical Care Services. In addition to the pharmaceutical care requirements for the pharmacy's specific license classification, the following requirements must be met.

(A) Sterile pharmaceuticals compounded pursuant to prescription drug orders (outpatients and long-term care facility patients).

(i) Primary provider. There shall be a designated physician primarily responsible for the patient's medical care. There shall be a clear understanding between the physician, the patient, and the pharmacy of the responsibilities of each in the areas of the delivery of care, and the monitoring of the patient. This shall be documented in the patient medication record (PMR).

(ii) Patient training. The pharmacist-in-charge shall develop policies that assure that the patient and/or patient's caregiver receives information regarding drugs and their safe and appropriate use, including instruction regarding:

(I) appropriate disposition of hazardous solutions and ancillary supplies;

(II) proper disposition of controlled substances in the home;

(III) self-administration of drugs, where appropriate;

(IV) emergency procedures, including how to contact an appropriate individual in the event of problems or emergencies related to drug therapy; and

(V) if the patient or patient's caregiver prepares sterile preparations in the home, the following additional information shall be provided:

(-a-) safeguards against microbial contamination, including aseptic techniques for compounding intravenous admixtures and aseptic techniques for injecting additives to premixed intravenous solutions;

(-b-) appropriate storage methods, including storage durations for sterile pharmaceuticals and expirations of self-mixed solutions;

(-c-) handling and disposition of premixed and self-mixed intravenous admixtures; and

(-d-) proper disposition of intravenous admixture compounding supplies such as syringes, vials, ampules, and intravenous solution containers.

(iii) Pharmacist-patient relationship. It is imperative that a pharmacist-patient relationship be established and maintained throughout the patient's course of therapy. This shall be documented in the patient's medication record (PMR).

(iv) Patient monitoring. The pharmacist-in-charge shall develop policies to ensure that:

(I) the patient's response to drug therapy is monitored and conveyed to the appropriate health care provider; and

(II) the first dose of any new drug therapy is administered in the presence of an individual qualified to monitor for and respond to adverse drug reactions.

(B) Sterile pharmaceutical compounded pursuant to medication orders (inpatients).

(i) Education. The pharmacist-in-charge in cooperation with appropriate multi-disciplinary staff of the facility shall develop policies that assure that:

(I) the patient and/or patient’s caregiver receives information regarding drugs and their safe and appropriate use; and

(II) health care providers are provided with patient specific drug information.

(ii) Patient monitoring. The pharmacist-in-charge in cooperation with appropriate multi-disciplinary staff of the facility shall develop policies to ensure that the patient’s response to drug therapy is monitored and conveyed to the appropriate health care provider.

(8) Drugs, components, and materials used in sterile compounding.

(A) Drugs used in sterile compounding shall preferably be a USP/NF grade

substances manufactured in an FDA-registered facility.

(B) If USP/NF grade substances are not available shall be of a chemical grade in one of the following categories:
  (i) Chemically Pure (CP);
  (ii) Analytical Reagent (AR); or
  (iii) American Chemical Society (ACS); or
  (iv) Food Chemical Codex; or

(C) If a drug, component or material is not purchased from a FDA-registered facility, the pharmacist shall establish purity and stability by obtaining a Certificate of Analysis from the supplier.

(D) All components shall:
  (i) preferably be manufactured in an FDA-registered facility; or
  (ii) in the professional judgment of the pharmacist, be of high quality and obtained from acceptable and reliable alternative sources; and
  (iii) stored in properly labeled containers in a clean, dry area, under proper temperatures.

(E) Drug product containers and closures shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the compounded drug product beyond the desired result.

(F) Components, drug product containers, and closures shall be rotated so that the oldest stock is used first.

(G) Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the compounded drug product.

(H) A pharmacy may not compound a drug product which appears on an official federal Food and Drug Administration list of drug products withdrawn or removed from the market because they are found to be unsafe or not effective.

(9) Compounding process.

(A) All significant procedures performed in the compounding area shall be covered by written SOPs designed to ensure accountability, accuracy, quality, safety, and uniformity in the compounding process. At a minimum, SOPs shall be developed for:
  (i) the facility;
  (ii) equipment;
  (iii) personnel;
  (iv) actual compounding;
  (v) product evaluation;
  (vi) packaging; and
  (vii) storage of compounded pharmaceuticals.

(B) Any compounded pharmaceutical with an official monograph in the USP/NF shall be compounded, labeled, and packaged in conformity with the USP/NF monograph for the drug.

(C) Any person with an apparent illness or open lesion that may adversely affect the safety or quality of a drug product being compounded shall be excluded from direct contact with components, drug product containers, closures, any materials involved in the compounding process, and drug products until the condition is corrected.

(D) Personnel engaged in the compounding of drug products shall wear clean clothing appropriate to the operation being performed. Protective apparel, such as coats/jackets, aprons, hair nets, gowns, hand or arm coverings, or masks shall be worn as necessary to protect personnel from chemical exposure and drug products from contamination.

(E) At each step of the compounding process, the pharmacist shall assure that components used in compounding are accurately weighed, measured, or subdivided as appropriate to conform to the formula being prepared.

(10) Quality control.

(A) Quality control procedures. The pharmacy shall follow established quality control

procedures to monitor the quality of compounded drug products for conformity with the quality indicators established for the product. When developing these procedures, pharmacy personnel shall consider the provisions of Chapter 797, concerning Pharmaceutical Compounding - Sterile Preparations, Chapter 1075, concerning Good Compounding Practices, and Chapter 1160, concerning Pharmaceutical Calculations in Prescription Compounding contained in the current USP/NF. Such procedures shall be documented in the sterile compounding record.

(B) End product evaluations.

(i) The pharmacy shall conduct and document end product evaluations appropriate for the preparation in accordance with written SOPs. End product evaluations for non-batch compounded pharmaceuticals may be performed on random samples. All batch compounded pharmaceuticals shall have end product evaluations.

(ii) High-risk level compounded sterile pharmaceutical for administration by injection into the vascular and central nervous systems that are prepared in groups of more than 25 identical individual single-dose packages (such as ampuls, bags, syringes, and vials), or in multiple dose vials for administration to multiple patients, or are exposed longer than 12 hours at 2 - 8 degrees Celsius (36 - 46 degrees Fahrenheit) and longer than six hours at warmer than 8 degrees Celsius (46 degrees Fahrenheit) before they are sterilized shall be tested to ensure they are sterile and do not contain excessive bacterial endotoxins and if a suspension, is not contaminated by fungus.

(e) Records.

(1) Maintenance of records. Every record required by this section shall be kept by the pharmacy for at least two years.

(2) Compounding records when compounding pursuant to patient specific prescription drug or medication orders. Compounding records for all compounded pharmaceuticals shall be maintained by the pharmacy electronically or manually as part of the prescription drug or medication order, formula record, formula book, or compounding log and shall include:

(A) the date of preparation;

(B) a complete formula, including methodology and necessary equipment which includes the brand name(s) of the raw materials, or if no brand name, the generic name(s) and name(s) of the manufacturer(s) of the raw materials and the quantities of each;

(C) signature or initials of the pharmacist or pharmacy technician performing the compounding;

(D) signature or initials of the pharmacist responsible for supervising pharmacy technicians and other supportive personnel and conducting in-process and finals checks of compounded pharmaceuticals if pharmacy technicians perform the compounding function;

(E) the quantity in units of finished products or grams of raw materials;

(F) the package size and the number of units prepared;

(G) the criteria used to determine the beyond-use date; and

(H) documentation of performance of quality control procedures.